

Nominations from FDA's Center for Drug Evaluation and Research

Senna Study using the p53 hemizygous Mouse Model (CDER; High Priority)

The safety of stimulant laxatives is current being reassessed by CDER as a result of rodent carcinogenicity findings for phenolphthalein in 2-year mouse and rat studies and confirmatory results in the p53 hemizygous mouse. As a result of these findings, phenolphthalein was removed from the OTC market. CDER is requesting a p53 hemizygous study to compliment a 2-year rat study that will be conducted for Senna. Senna has been reported as positive in the Ames test. A limited rat study of 2 years duration was performed, although there were fewer animals per group (20) than in a standard study and histopathological analysis focused only on GI. This study showed an early increase in lymph node hyperplasia, but at study termination there was no difference in tumors of hyperplasia between control and treated groups. Thus, the carcinogenic potential of this widely used laxative is unknown and the planned 2-year rat bioassay has yet to be initiated.